Evaluation of the platelet function analyzer (PFA-100®) vs. the thromboelastogram (TEG) in the parturient

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Background: The platelet function analyzer (PFA-100®) is a bedside test of coagulation designed to evaluate platelet function. It measures the time required for whole blood to occlude a membrane impregnated with either epinephrine (EPI) or adenosine 5′diphosphate (ADP). The results are reported as closure time (CT-EPI or CT-ADP) in seconds. The thromboelastogram (TEG) measures whole blood clotting and the maximum amplitude (MA) correlates with platelet count and function. We wished to establish whether there is a correlation between the CT and platelet count, between the CT and MA, and between the MA and platelet count.

Methods: Platelet count, CT, and MA were measured in blood drawn from 172 healthy term parturients using the PFA-100®.

Results: We were unable to detect a significant correlation between the CT-EPI and platelet count ($r = -0.1$, $P = 0.21$), or the CT-ADP and platelet count ($r = -0.02$, $P = 0.83$). We also did not find a correlation between the CT-EPI and MA ($r = -0.13$, $P = 0.12$) or between the CT-ADP and MA ($r = -0.11$, $P = 0.19$). However, we found a significant correlation between platelet count and MA ($r = 0.33$, $P < 0.001$).

Conclusions: We conclude that the CT does not correlate with the platelet count or MA in the parturient, but the TEG does. Therefore the TEG may be a better tool to evaluate coagulation in the parturient with thrombocytopenia.

Keywords: Platelets; Epidural hematoma; Platelet Function Analyzer (PFA-100®); Thromboelastogram

INTRODUCTION

Thrombocytopenia is a relative contraindication to neuraxial anesthesia. Although there are no data to support an absolute platelet count below which neuraxial anesthesia is contraindicated, approximately 30% of anesthesiologists in the United Kingdom regard epidural insertion as contraindicated when the platelet count is <100 × 10^9/L. The platelet function analyzer (PFA-100®, Dade Behring, Newark, Delaware, USA) is a relatively new commercially available bedside test of coagulation that is specifically designed to evaluate platelet function. The machine simulates the in-vivo hemostatic mechanism of platelet function by accelerating citrated whole blood through a small aperture cut in a collagen membrane of a test cartridge. The collagen membrane is coated with one of two platelet activators, epinephrine (EPI) or adenosine 5′diphosphate (ADP). The time for the blood to occlude the aperture is called the closure time (CT) and estimates platelet function. The thromboelastogram (TEG) measures the shear elasticity of clotting blood and provides information about all phases of coagulation and fibrinolysis, and assesses platelet function in a short time while using <1 mL of a whole blood sample. The maximum amplitude (MA), a parameter measured by the TEG, has been found to correlate best with platelet count and function.
Vincelot et al.\textsuperscript{5} evaluated the PFA-100\textsuperscript{®} in women with thrombocytopenia and those with preeclampsia. They were not able to find a correlation between the platelet count and CT in the parturient with or without thrombocytopenia. They found a difference in the CT between those with thrombocytopenia and those without, but their evaluation was based on a platelet count $<150 \times 10^9/L$ and the principal clinical concern is when the platelet count is $<100 \times 10^9/L$. Furthermore they did not compare the results of the PFA-100\textsuperscript{®} to another test of platelet function.

The purpose of this study was to determine in the parturient (1) if there is a correlation between the platelet count and CT, (2) if there is a difference in CT between parturients with a platelet count $\geq 100 \times 10^9/L$ vs. those with a platelet count $<100 \times 10^9/L$, and (3) to determine if there is a correlation between the CT and the MA. A correlation between the platelet count and the PFA-100\textsuperscript{®} or between the CT and the MA would imply that the machine may be helpful in the clinical arena when evaluating coagulation in the parturient with thrombocytopenia who requests labor neuraxial analgesia.

**METHODS**

The protocol was approved by the Institutional Review Board of the Mount Sinai School of Medicine of New York University. All subjects were otherwise healthy women who had no known medical problems, were not taking any medications, were at least 37 week’s pregnant and were undergoing a vaginal or cesarean delivery.

After each subject had given written informed consent, blood was drawn into a tube containing 3.8% (0.129M) buffered sodium citrate solution. The blood sample was analyzed within 20 min in the PFA-100\textsuperscript{®} for CT with both the EPI and ADP cartridges, and in the TEG with specific focus on MA. Thromboelastography was performed with a 5000 series TEG\textsuperscript{®} analyzer (Haemoscope Corp., Skokie, IL) and celite activation. Hemoglobin concentration and platelet count were measured at the same time, on a different sample of blood drawn simultaneously, in the hematology laboratory using a Coulter counter. Obstetric outcome (vaginal vs. cesarean delivery) and whether the patient had neuraxial anesthesia were also recorded.

**Statistical analysis**

A correlation between the platelet count and CT, between the platelet count and MA, and between CT and MA were sought using Spearman’s rank correlation coefficient ($r$). The Wilcoxon rank-sum test was used to assess if there was a statistically significant difference in CT or MA with a platelet count $\geq 100 \times 10^9/L$ vs. a platelet count $<100 \times 10^9/L$. Results are presented as median and range except where otherwise noted. Differences were considered statistically significant at $P < 0.05$.

**RESULTS**

We enrolled 182 patients and studied 172. We were unable to obtain blood from 10 patients. After we collected blood from 160 patients we noted that only six had a platelet count $<100 \times 10^9/L$. Therefore, we decided to continue to enroll only those who had a platelet count $<100 \times 10^9/L$. The median age of the patients was 33 years with a range of 18–49. Most patients (69%) were Caucasian, 13% Hispanic, 8% African American, 7% Asian, and 3% other ethnicity.

For the entire group of 172 patients, the median platelet count was 192 $00 \times 10^9/L$, range 44–471, hemoglobin concentration 12.4 g/dL, CT-EPI 141 s, CT-ADP 99 s, and MA 68 mm. There were 18 patients whose platelet count was $<100 \times 10^9/L$. We were unable to detect a significant correlation between the CT-EPI and platelet count ($r = -0.1$, $P = 0.21$) or the CT-ADP and platelet count ($r = -0.02$, $P = 0.83$) (Figs. 1 and 2). There was no statistically significant difference between the CT-EPI or CT-ADP in those with a platelet count $\geq 100 \times 10^9/L$ (CT-EPI 141 s, CT-ADP 99) vs. those with a platelet count $<100 \times 10^9/L$ (CT-EPI 152 s, CT-ADP 93) (Table 1). We also failed to find a correlation between the CT and the MA (Figs. 3 and 4). We found a significant correlation between platelet count and MA ($r = 0.33$, $P < 0.001$) (Fig. 5), and a difference in MA that did not quite reach statistical significance, between those with a platelet count $\geq 100 \times 10^9/L$ (MA = 69) vs. those with a platelet count $<100 \times 10^9/L$ (MA = 68), $P = 0.06$ (Table 1).

For the blood samples of the 172 patients studied, the PFA-100\textsuperscript{®} generated an error message 26 times in 22 parturients, 17 with PFA-EPI and 9 with the PFA-ADP. The error messages and possible etiologies for the error are listed in Table 2. If there was sufficient blood available, a second attempt with that cartridge was made (7 in the PFA-EPI and 7 in the PFA-ADP). A second error occurred once with the PFA-EPI and three times with the PFA-ADP. These four assessments and the twelve for which there was insufficient blood for a second PFA evaluation were not included in the final analyses.

Forty-one percent of the patients had vaginal deliveries, and 59% cesarean deliveries. Neuraxial (spinal or epidural) anesthesia was used in 164/170 patients (96%), 76 (46%) received an epidural catheter, 79 (48%) received a spinal anesthetic, and 9 (5%) received a combined spinal-epidural technique (data missing for 2 patients). Of the 18 patients with a platelet count $<100 \times 10^9/L$, 5 did not receive an epidural anesthetic. The platelet counts in these five patients were $44 \times 10^9/L$, $56 \times 10^9/L$, $86 \times 10^9/L$, and two patients who had a platelet count of $97 \times 10^9/L$.
Three patients had platelet counts <75 · 10^9/L and received epidural anesthesia. The platelet counts in these three patients were 62 · 10^9/L, 65 · 10^9/L, and 72 · 10^9/L. There were no cases of epidural hematoma in any of the enrolled patients.

DISCUSSION

We were unable to find a significant correlation between the CT with either the EPI or ADP cartridge and the platelet count among parturients across a wide range of platelet counts (44–471 · 10^9/L). Furthermore, we were unable to find any difference in the CT between patients with a platelet count <100 · 10^9/L and those with a platelet count ≥ 100 · 10^9/L, and we did not find a correlation between the CT and the MA. However, we found a significant correlation between the platelet count and MA.

Thrombocytopenia is the most common hematologic disorder during pregnancy. Platelets play an important role in the hemostatic system. They initiate the hemostatic
Fig. 3  Graph of the closure time with the platelet function analyzer using the adenosine 5’diphosphate (CT-ADP) cartridge vs. the maximum amplitude (MA) from the thromboelastogram.  

Fig. 4  Graph of the closure time with the platelet function analyzer using the epinephrine (CT-EPI) cartridge vs. the maximum amplitude (MA) from the thromboelastogram.  

Fig. 5  Graph of platelet count (×10⁹/L) vs. the maximum amplitude (MA) from the thromboelastogram.
process by aggregating and forming a platelet plug, and the entire coagulation cascade takes place on the platelet membrane. Commonly used tests of platelet function include the bleeding time (BT) and TEG.

BT is a simple bedside test that should be able to evaluate both the quality and quantity of the platelets. This test, however, is no longer considered useful in determining the safety of epidural catheter placement because it does not predict the risk of bleeding at other sites, and because there is wide observer variability.

The TEG can measure all phases of coagulation and fibrinolysis in a single sample of blood. Consistent with the results of Orlikowsky et al. we found a correlation between the MA and the platelet count. Although there is no evidence that a normal TEG can predict the safety of epidural anesthesia, it does provide information about the adequacy of platelet function in a relatively short time.

The PFA-100® could be an ideal test for the parturient because it is specific for evaluating platelet function, and platelet disorders are commonly found in the parturient. The machine would provide an ideal bedside test of coagulation for use by the anesthesiologist because only a small amount of whole blood is needed (500 µl) and the test results are available within 5 min. Results of the PFA-100®, in the non-parturient, correlate with aggregometry, which is the gold standard for assessment of platelet function, and is sensitive for the detection of von Willebrand disease and platelet disorders caused by acetylsalicylic acid.

We are aware of only one other published study that has evaluated the PFA-100® in the parturient. Similar to those results, we were unable to find a correlation between platelet count and CT in the otherwise healthy parturient, with or without thrombocytopenia. We also did not find a correlation between the CT and the MA, a parameter known to correlate with platelet function. Vincelot et al. however, did find a correlation between the PFA-ADP and platelet count in women who had preeclampsia and thrombocytopenia. In another study, Warren et al. also found that the CT-ADP and the CT-EPI increased along with the severity of preeclampsia, although the CT did not correlate with clinical bleeding.

This patient group, preeclampsia and thrombocytopenia, was not a part of our study.

A problem we noted with the platelet function analyzer was the number of error messages generated. We had 26 error messages (8%) in 344 test attempts. Ignoring the three errors for insufficient sample (possible “user error”) this represents 7% of the samples. The errors occurred throughout the study and were not over-represented when we first started using the machine, thus unfamiliarity is an unlikely reason for the errors. We do not know if others have encountered a similar incidence of errors.

The overall risk of epidural or spinal hematoma following neuraxial anesthesia is in the range of 1:150 000–220 000. We are aware of 12 reports in the literature of neuraxial (spinal or epidural) hematoma occurring in the parturient. Three of these occurred in women with preeclampsia and thrombocytopenia. In one report the platelet count was 71 × 10⁹/L and in the other two, the platelet count was not reported. Therefore, caution must be used when one is faced with the decision of placing a neuraxial anesthetic in the patient with thrombocytopenia, and a machine that evaluates platelet function would be useful.

Bedside monitors of coagulation could be used in one of two ways, as the only test of coagulation status (i.e., abandoning use of the platelet count) or as a secondary test when the platelet count is abnormal. Based on the results of our study it is unlikely that the PFA-100® could be used in either way. Not only was there no correlation between PFA and platelet count, there was also no correlation between PFA and the MA from the TEG, a variable that correlates with platelet count and function. Alternatively, the TEG may be promising in evaluating coagulation in the parturient with thrombocytopenia since we found, as have others, that it correlates with platelet count. We recommend further study should be done with the TEG among thrombocytopenic parturients.

Although we did not have any epidural hematomas in our study group, including the 18 patients with a platelet count <100 × 10⁹/L, there are too few patients to make a definitive statement as to the safety of neuraxial anesthesia in the presence of thrombocytopenia.

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<th>Table 2. Error messages and their possible etiology*</th>
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<td>Error message</td>
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<td>---------------------------------</td>
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<tr>
<td>Flow obstruction</td>
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<td>Maximum test time exceeded</td>
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<tr>
<td>Air leak</td>
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<tr>
<td>Maximum syringe travel reached</td>
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<td>Insufficient sample</td>
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*PFA-100®, Platelet Function Analyzer operating manual, Newark, Delaware, USA.
In conclusion, we were unable to find a correlation between CT with the PFA-100® and the platelet count or CT and MA, but we did find a correlation between platelet count and MA. Due to the very low incidence of epidural hematoma it is unlikely that any test would be able to predict the possibility of epidural hematoma. However, the TEG seems promising in this regard whereas the PFA-100® does not, and we recommend additional study with the TEG. Until a bedside test is found that can be used to predict platelet count, and more importantly the possibility of epidural hematoma, individual clinical assessment including determining if the patient has a history of bruising or bleeding, and the absolute and trend in platelet count, remain the best method for evaluating coagulation in the patient with thrombocytopenia who requests labor neuraxial analgesia.

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REFERENCES